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Prostate Cancer Early Detection, Diagnosis, and Staging

Learn about the signs and symptoms of prostate cancer. Find out how prostate cancer is tested for, diagnosed, and staged.

Finding Prostate Cancer Early

Catching cancer early often allows for more treatment options. Some early cancers

It's not clear from studies if benefits of screening outweigh the risks

Doctors are still studying if screening will lower the risk of death from prostate cancer. The results from 2 large studies have been conflicting, and they have not offered clear answers.

- Results from a large study done in the United States found that annual screening
 with PSA and DRE did detect more prostate cancers than in men not screened, but
 this screening did not lower the death rate from prostate cancer. However,
 questions have been raised about this study, because some men in the nonscreening group actually were screened during the study, which might have
 affected the results.
- A large European study did find a lower risk of death from prostate cancer with PSA screening (done about once every 4 years), but the researchers estimated that about 570 men would need to be invited to be screened (and 18 cancers would need to be detected) to prevent one death from prostate cancer.
- So far, neither of these studies has shown that PSA screening helps men live longer overall (that is, that it lowers the overall death rate).

Both of these studies are being continued to see if longer follow-up will give clearer results. Prostate cancer screening is being explored in several other large studies as well.

For now, the American Cancer Society recommends that men thinking about getting screened for prostate cancer learn as much as they can so they can make an informed decision based on available information, discussions with their health care provider, and their own views on the possible benefits, risks, and limits of screening. (To learn more, see American Cancer Society Recommendations for Prostate Cancer Early Detection.)

Until more information is available, you and your health care provider should decide whether you should be screened for prostate cancer. There are many factors to take into account, including your age, health, and family history. For example, you might feel it's more important to be screened if prostate cancer runs in your family.

If you're younger and develop prostate cancer, it may shorten your life if it's not caught early. Screening men who are much older or in poor health is less likely to be helpful. This is because most prostate cancers are slow-growing, and men who are older or have major health problems are often more likely to die from other causes before their prostate cancer grows enough to cause problems.

Hyperlinks

1. www.cancer.org/cancer/types/prostate-cancer/treating/watchful-waiting.html

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Screening Tests for Prostate Cancer

Screening is testing to find cancer in people before they have symptoms. At this time, it's not clear if the benefits of prostate cancer screening outweigh the risks for most men. Still, after discussing the pros and cons of screening with their doctors, some men might reasonably choose to be screened.

other than cancer can also affect PSA levels.

Factors that might raise PSA levels include:

- Older age: PSA levels normally go up slowly as you get older, even if your prostate is normal.
- Having an enlarged prostate: Conditions such as benign prostatic hyperplasia (BPH), a non-cancerous enlargement of the prostate that affects many men as they grow older, can raise PSA levels.
- **Prostatitis:** This is an infection or inflammation of the prostate gland, which can raise PSA levels.
- **Ejaculation:** This can make the PSA go up for a short time. This is why some doctors suggest that men abstain from ejaculation for a day or two before testing.
- Riding a bicycle: Some studies have suggested that cycling may raise PSA levels for a short time (possibly because the seat puts pressure on the prostate), although not all studies have found this.
- Certain urologic procedures: Some procedures done in a doctor's office that affect the prostate, such as a prostate biopsy or cystoscopy, can raise PSA levels for a short time. Some studies have suggested that a digital rectal exam (DRE) might raise PSA levels slightly, although other studies have not found this. Still, if both a PSA test and a DRE are being done during a doctor visit, some doctors advise having the blood drawn for the PSA before having the DRE, just in case.
- **Certain medicines:** Taking male hormones like testosterone (or other medicines that raise testosterone levels) may cause a rise in PSA.

Some things might **lower PSA levels** (even if a man has prostate cancer):

- 5-alpha reductase inhibitors: Certain drugs used to treat BPH or urinary symptoms, such as finasteride (Proscar or Propecia) or dutasteride (Avodart), can lower PSA levels. These drugs can also affect prostate cancer risk (discussed in Can Prostate Cancer Be Prevented?¹. Tell your doctor if you are taking one of these medicines. Because they can lower PSA levels, the doctor might need to adjust for this.
- **Herbal mixtures:** Some mixtures that are sold as dietary supplements might mask a high PSA level. This is why it's important to let your doctor know if you are taking any type of supplement, even ones that are not necessarily meant for prostate health. Saw palmetto (an herb used by some men to treat BPH) does not seem to affect PSA.

• Certain other medicines: Some research has suggested that long-term use of certain medicines, such as aspirin, statins (cholesterol-lowering drugs), and thiazide diuretics (such as hydrochlorothiazide) might lower PSA levels. More research is needed to confirm these findings.

For men who are thinking about being screened for prostate cancer, it's important to talk to your doctor about anything you're taking that might affect your PSA level, as it might affect the accuracy of your test result.

A word about at-home PSA tests

Some companies now offer PSA test kits that let you collect a blood sample at home (typically from a finger stick) and then send it to a lab for testing. This could be more convenient for some men, and it might even allow some men to be tested who otherwise might not be.

However, a drawback with at-home testing is that it might not give a man the chance to discuss the pros and cons of prostate cancer screening with a health care provider before being tested, which could help him make an informed decision on whether to be screened. This shared decision making is an important part of the American Cancer Society Recommendations for Prostate Cancer Early Detection.

Another important issue is that PSA blood test results are not black and white – that is, the test can't tell for sure that you have (or don't have) prostate cancer. It's important to discuss the test results with a health professional who understands what the results mean for you.

Special types of PSA tests

The PSA level from a screening test is sometimes referred to as **total PSA**, because it includes all forms of PSA (described below). If you decide to get a PSA screening test and the result isn't normal, some doctors might consider using different types of PSA tests to help decide if you need a prostate biopsy, although not all doctors agree on how to use these tests. If your PSA test result isn't normal, ask your doctor about what it means for your prostate cancer risk and your need for further tests.

Percent-free PSA: PSA occurs in 2 major forms in the blood. One form is attached ("complexed") to blood proteins, while the other circulates free (unattached). The percent-free PSA (%fPSA), also known as the free/total PSA ratio (f/t PSA), is the ratio of how much PSA circulates free compared to the total PSA level. The percent-free PSA

is lower in men who have prostate cancer than in men who do not.

If your PSA test result is in the borderline range (between 4 and 10), the percent-free PSA might be used to help decide if you should have a prostate biopsy. A *lower* percent-free PSA means that your chance of having prostate cancer is higher and you should probably have a biopsy.

Many doctors recommend a prostate biopsy for men whose percent-free PSA is 10% or less, and advise that men consider a biopsy if it is between 10% and 25%. Using these cutoffs detects most cancers and helps some men avoid unnecessary biopsies. This test is widely used, but not all doctors agree that 25% is the best cutoff point to decide on a biopsy, and the cutoff may change depending on the overall PSA level.

Complexed PSA: This test directly measures the amount of PSA that is attached to other proteins (the portion of PSA that is not "free"). This test could be done instead of checking the total and free PSA, and it could give the same amount of information, but it is not widely used.

Tests that combine different types of PSA: Some newer tests combine the results of different types of PSA to get an overall score that reflects the chance a man has prostate cancer (particularly cancer that might need treatment). These tests include:

- The **Prostate Health Index (PHI)**, which combines the results of total PSA, free PSA, and proPSA
- The **4Kscore test**, which combines the results of total PSA, free PSA, intact PSA, and human kallikrein 2 (hK2), along with some other factors
- The **IsoPSA test**, which looks at different forms of PSA proteins in the blood to help determine if they came from cancer cells

These tests might be useful in men with a slightly elevated PSA, to help determine if they should have a prostate biopsy. Some of these tests might also be used to help determine if a man who has already had a prostate biopsy that didn't find cancer should have another biopsy.

PSA velocity: The PSA velocity is not a separate test. It is a measure of how fast the PSA rises over time. Normally, PSA levels go up slowly with age. Some research has found that these levels go up faster if a man has cancer, but studies have not shown that the PSA velocity is more helpful than the PSA level itself in finding prostate cancer. For this reason, most doctors do not use PSA velocity as part of screening for prostate cancer.

PSA density: PSA levels are higher in men with larger prostate glands. The PSA density (PSAD) is sometimes used for men with large prostate glands to try to adjust for this. The doctor measures the volume (size) of the prostate gland with transrectal ultrasound (TRUS, discussed in Tests to Diagnose and Stage Prostate Cancer) and divides the PSA number by the prostate volume. A higher PSA density indicates a greater likelihood of cancer. PSA density appears to be about as accurate as the percent-free PSA test, although a drawback is that it requires that an ultrasound is done.

Age-specific PSA ranges: PSA levels are normally higher in older men than in younger men, even when there is no cancer. A PSA result within the borderline range might be more worrisome in a 50-year-old man than in an 80-year-old man. For this reason, some doctors have suggested comparing PSA results with results from other men of the same age. But the usefulness of age-specific PSA ranges is not well proven, so most doctors and professional organizations do not recommend their use at this time.

Digital rectal exam (DRE)

For a digital rectal exam (DRE), the doctor inserts a gloved, lubricated finger into the rectum to feel for any bumps or hard areas on the prostate that might be cancer. As shown in the picture below, the prostate is just in front of the rectum. Prostate cancers often begin in the back part of the gland, and can sometimes be felt during a rectal exam. This exam can be uncomfortable (especially for men who have hemorrhoids), but it usually isn't painful and only takes a short time.

• Your own comfort level with waiting or getting further tests

If your initial PSA test was ordered by your primary care provider, you may be referred to a **urologist** (a doctor who treats diseases of the genital and urinary tract, including prostate cancer) for this discussion or for further testing.

Repeating the PSA test

A man's blood PSA level can vary over time (for a number of reasons), so some doctors recommend repeating the test after a month or so if the initial PSA result is abnormal. This is most likely to be a reasonable option if the PSA level is on the lower end of the borderline range (typically 4 to 7 ng/mL). For higher PSA levels, doctors are more likely to recommend getting other tests, or going straight to a prostate biopsy.

Getting other tests

If the initial PSA result is abnormal, another option might be to get another type of test (or tests) to help you and your doctor get a better idea if you might have prostate cancer (and therefore need a biopsy). Some of the tests that might be done include:

A digital rectal exam (DRE), if it hasn't been done already
 One or more of the other special types of PSA tests discussed above, such as
 the Prostate Health Index (PHI), 4Kscore test, IsoPSA, or percent-free PSA; or
 other lab tests, such as the ExoDx Prostate(IntelliScore) or SelectMDx (described)

For more details on the prostate biopsy and how it is done, see Tests to Diagnose and Stage Prostate Cancer

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/causes-risks-prevention/prevention.html</u>
- 2. www.cancer.org/cancer/types/prostate-cancer/about/new-research.html

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Because prostate cancer often grows slowly, men without symptoms of prostate cancer who have less than a 10-year life expectancy should not be offered prostate cancer screening, because they aren't likely to benefit from it. Overall health status, and not age alone, is important when making decisions about screening.

Even after a decision about testing has been made, the discussion about the pros and cons of testing should be repeated as new information about the benefits and risks of testing becomes available. Further discussions are also needed to take into account changes in a man's health, values, and preferences.

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Insurance Coverage for Prostate Cancer Screening

The American Cancer Society (ACS) supports legislation assuring that men have insurance coverage for prostate screening exams.

- Men should have the option of screening
- State efforts to ensure prostate cancer screening coverage
- Medicare coverage
- Medicaid coverage

Men should have the option of screening

ACS recognizes that it's not yet clear whether screening lowers the risk of dying from prostate cancer. Until such time when studies are conclusive, men and their doctors

should be free to determine if testing is right for them. Men shouldn't be prevented from getting prostate cancer screening because of testing costs, lack of health insurance coverage, or lack of access to testing.

ACS doesn't recommend routine screening for prostate cancer for all men at this time, because we believe proper guidance and education is needed before testing is done. Doctors and other health care providers should help men understand the potential risks and benefits of prostate-specific antigen (PSA) testing, allowing them to make an informed decision on testing.

State efforts to ensure prostate cancer screening coverage

Many states have laws requiring private health insurers to cover tests to detect prostate cancer, including the PSA test and digital rectal exam (DRE). Some states also assure that public employee benefit health plans provide coverage for prostate cancer screening tests.

Most state laws assure annual coverage for men ages 50 and over and for high-risk men, ages 40 and over. "High-risk men" typically refers to African American men and/or men with a family history of prostate cancer. Some states have slightly different coverage requirements.

Laws on coverage vary from state to state, so check with your insurer or with your state insurance commissioner's office to learn what's covered.

Medicare coverage

Medicare covers a PSA blood test and a DRE once a year for all men with Medicare age 50 and over.

PSA test: You pay nothing for a yearly PSA blood test. If you get the test from a doctor who doesn't accept assignment, you may have to pay a fee for the doctor's services, but not for the test itself.

Digital rectal exam: If your doctor does this test, you pay 20% of the Medicare-approved amount for a yearly DRE and for your doctor's services related to the exam. The Part B deductible applies. If the DRE is done in a hospital outpatient setting, there is a copayment.

Medicaid coverage

Medicaid coverage of prostate cancer screening varies by state.

People who qualify for Medicaid based on their state's decision to expand Medicaid under the Affordable Care Act (ACA)¹ are entitled to the same screening services as people covered by private insurance.

For people who qualify for Medicaid based on other pathways, prostate cancer screening coverage is determined by the state. Most Medicaid programs do cover screening.

To learn more about prostate cancer screening coverage in your state, contact <u>your</u> state's Medicaid office².

Hyperlinks

- 1. <u>www.cancer.org/cancer/financial-insurance-matters/health-insurance-laws/the-health-care-law.html</u>
- 2. www.medicaid.gov/state-overviews/index.html

References

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Signs and Symptoms of Prostate Cancer

Most prostate cancers are found early, through screening.

Early prostate cancer usually causes no symptoms. While not common, symptoms of early prostate cancer might include:

- Problems urinating, including a slow or weak urinary stream or the need to urinate more often, especially at night
- Blood in the urine or semen

Along with the symptoms above, **more advanced prostate cancer** can sometimes cause other symptoms, such as:

- Trouble getting an erection (erectile dysfunction or ED)
- Pain in the hips, back (spine), chest (ribs), or other areas, from cancer that has spread to the bones
- Weakness or numbness in the legs or feet, or even loss of bladder or bowel control, from cancer in the spine pressing on the spinal cord
- Weight loss
- Feeling very tired

Most of these symptoms are more likely to be caused by something other than prostate cancer. For example, trouble urinating is much more often caused by benign prostatic hyperplasia (BPH), a non-cancerous growth of the prostate.

Still, it's important to tell your health care provider if you have any of these symptoms so that the cause can be found and treated, if needed. Some men might need more tests to check for prostate cancer.

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diagnosis-of-prostate-cancer on July 12, 2023.

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Tests to Diagnose and Stage Prostate Cancer

Most prostate cancers are first found as a result of screening. (See Screening Tests for Prostate Cancer.) Early prostate cancers usually don't cause symptoms, but more advanced cancers are sometimes first found because of symptoms they cause.

If prostate cancer is suspected based on results of screening tests or symptoms, tests will be needed to be sure. If you're seeing your primary care doctor, you might be referred to a **urologist**, a doctor who treats diseases of the genital and urinary tract, including prostate cancer.

The actual diagnosis of prostate cancer can only be made with a prostate biopsy (discussed below).

- Medical history and physical exam
- PSA blood test
- Prostate biopsy
- Testing prostate cancer cells for gene or protein changes
- Genetic testing for some men with prostate cancer
- Imaging tests for prostate cancer
- Lymph node biopsy

Medical history and physical exam

If your doctor suspects you might have prostate cancer, you will be asked about any symptoms you are having, such as urinary or sexual problems, and how long you have had them. You might also be asked about possible <u>risk factors</u>¹, including your family history.

Your doctor will also examine you. This might include a digital rectal exam (DRE), during which the doctor inserts a gloved, lubricated finger into your rectum to feel for

any bumps or hard areas on the prostate that might be cancer. If you do have cancer, the DRE can sometimes help tell if it's only on one side of the prostate, if it's on both sides, or if it's likely to have spread beyond the prostate to nearby structures. Your doctor may also examine other areas of your body.

After the exam, your doctor might order some tests.

PSA blood test

Prostate-specific antigen (PSA) is a protein made by cells in the prostate gland (both normal cells and cancer cells). PSA is mostly in semen, but a small amount is also in the blood.

Use in men who might have prostate cancer

The PSA blood test can be used to screen for prostate cancer in men without symptoms. It's also one of the first tests done in men who have symptoms that might be caused by prostate cancer.

PSA in the blood is measured in units called nanograms per milliliter (ng/mL). The ch /GSi

device inserts and removes the needle in a fraction of a second. Most doctors who do the biopsy will numb the area first by injecting a local anesthetic alongside the prostate. You might want to ask your doctor if there are plans to do this.

The biopsy itself takes about 10 minutes and is usually done in the doctor's office. You will likely be given antibiotics to take before the biopsy and possibly for a day or 2 after to reduce the risk of infection.

For a few days after the procedure, you may feel some soreness in the area and might notice blood in your urine. You may also have some light bleeding from your rectum, especially if you have hemorrhoids. Many men notice blood in their semen or have rust-colored semen, which can last for several weeks after the biopsy, depending on how often you ejaculate.

Getting the results of the biopsy

Your biopsy samples will be sent to a lab, where a doctor with special training, called a **pathologist**, will look at them with a microscope to see if they contain cancer cells. Getting the results (in the form of a pathology report) usually takes 1 to 3 days, but it can sometimes take longer. The results might be reported as:

- **Negative for cancer:** No cancer cells were seen in the biopsy samples.
- Positive for cancer: Cancer cells were seen in the biopsy samples.
- **Suspicious or atypical:** Something abnormal was seen, but it might not be cancer. (Different types of suspicious and atypical results are discussed below.)

If the biopsy is negative for cancer

If the prostate biopsy results are negative (that is, if they don't show cancer), and the chance that you have prostate cancer isn't very high based on your PSA level and other tests, you might not need any more tests, other than repeat PSA tests (and possibly DREs) sometime later.

But even if many samples are taken, biopsies can still sometimes miss a cancer if none of the biopsy needles pass through it. This is known as a **false-negative** result. If your doctor still strongly suspects you have prostate cancer (because your PSA level is very high, for example), they might suggest:

• Getting **other lab tests** (of blood, urine, or the prostate biopsy samples) to help get a better idea of if you might have prostate cancer. Examples of such tests include

the Prostate Health Index (PHI), 4Kscore test, PCA3 tests (such as Progensa), and ConfirmMDx. These tests are discussed in What's New in Prostate Cancer Research?⁴

- Getting an MRI of the prostate (described below) if it hasn't been done already) –
 which might show suspicious areas in the prostate that should be biopsied
- Getting a **repeat prostate biopsy**. This might include getting samples of parts of the prostate not biopsied the first time, or using imaging tests such as MRI to look more closely for abnormal areas to target.

the Gleason score is determined is modified to reflect the aggressive (fast-growing) nature of the cancer.

In theory, the Gleason score can be between 2 and 10, but scores below 6 are not often used.

Based on the Gleason score, prostate cancers are often divided into 3 groups:

- Cancers with a **Gleason score of 6 or less** may be called **well-differentiated** or **low-grade**. These cancers tend to grow slowly and are unlikely to spread. (In fact, some doctors have questioned whether these should even be called cancers.)
- Cancers with a Gleason score of 7 may be called moderately differentiated or intermediate-grade.
- Cancers with Gleason scores of 8 to 10 may be called poorly differentiated or high-grade.

Grade Groups

In recent years, doctors have come to realize that the Gleason score might not always be the best way to describe the grade of the cancer, for a couple of reasons:

- The outcomes for men with prostate cancer can be divided into more than just the 3 groups mentioned above. For example, men with a Gleason score of 3+4=7 cancer tend to do better than those with a 4+3=7 cancer. And men with a Gleason score of 8 cancer tend to do better than those with a Gleason score of 9 or 10.
- The scale of the Gleason score can be misleading for men with prostate cancer. For example, a man with a Gleason score of 6 cancer might assume that his cancer is in the middle of the range of grades (which in theory go from 2 to 10), even though grade 6 cancers are actually the lowest grade seen in practice. This might lead a man to think his cancer is more likely to grow and spread quickly, when grade 6 cancers typically do not spread or cause death. This misunderstanding could affect his decisions about treatment.

Because of this, doctors have developed **Grade Groups**, ranging from 1 (most likely to grow and spread slowly) to 5 (most likely to grow and spread quickly):

- Grade Group 1 = Gleason 6 (or less)
- Grade Group 2 = Gleason 3+4=7

- Grade Group 3 = Gleason 4+3=7
- Grade Group 4 = Gleason 8
- Grade Group 5 = Gleason 9-10

The Grade Groups will likely replace the Gleason score over time, but currently you might see either one (or both) on a biopsy pathology report.

Other information in a pathology report if cancer is found

Along with the grade of the cancer (if it is present), the pathology report often contains other information about the cancer, such as:

- The number of biopsy core samples that contain cancer (for example, "7 out of 12")
- The percentage of cancer in each of the cores
- Whether the cancer is on one side (left or right) of the prostate or on both sides (bilateral)

Suspicious, atypical, or other results

Sometimes a biopsy sample might not look like prostate cancer, but it doesn't look quite normal, either.

Prostatic intraepithelial neoplasia (PIN): In PIN, there are changes in how the prostate cells look, but the abnormal cells don't look like they've grown into other parts of the prostate (like cancer cells would). PIN is often divided into 2 groups:

- Low-grade PIN: The patterns of prostate cells appear almost normal.
- **High-grade PIN:** The patterns of cells look more abnormal.

Many men begin to develop **low-grade PIN** at an early age, but low-grade PIN is not thought to be related to prostate cancer risk. If low-grade PIN is reported on a prostate biopsy, your follow-up is usually the same as if nothing abnormal was seen.

If **high-grade PIN** is found on a biopsy, you might have a higher chance of developing prostate cancer over time. This is why doctors often watch men with high-grade PIN carefully and may advise another prostate biopsy (or lab tests to help determine the risk

different parts of the prostate (known as **multifocal high-grade PIN**), or if the original biopsy didn't take samples from all parts of the prostate.

Intraductal carcinoma: In intraductal carcinoma, prostate cancer (carcinoma) cells can be seen growing into pre-existing prostate ducts. This condition is often seen next to high-grade (fast-growing) prostate cancer.

If intraductal carcinoma is found on a prostate biopsy, there's a strong chance that there is high-grade prostate cancer near where the biopsy was taken from. Because of this, doctors often recommend treating the prostate with surgery or radiation therapy.

Atypical small acinar proliferation (ASAP): This might also be called **glandular atypia** or **atypical glandular proliferation**. It might also just be reported as "suspicious for cancer." All of these terms mean that there are cells in the biopsy sample that look like they might be cancer, but there are too few of them to be sure. If one of these terms is used, there's a high chance that there is also cancer in the prostate, which is why many doctors recommend getting another biopsy within a few months.

Proliferative inflammatory atrophy (PIA): In PIA, the prostate cells look smaller than normal, and there are signs of inflammation in the area. PIA is not cancer, and it's not yet clear if it leads to high-grade PIN or to prostate cancer directly.

Testing prostate cancer cells for gene or protein changes

If you have prostate cancer, the cancer cells from your biopsy might be tested for certain gene or protein changes that could affect your treatment options. For example:

If your cancer hasn't spread, your doctor might recommend a **molecular or genomic test** of your cancer cells to help determine how quickly the cancer is likely to grow and spread. Tests such as Decipher, Oncotype DX Prostate, Prolaris, and Promark can help you and your doctor decide if <u>active surveillance</u>⁵ might be right for you, or if treatment such as surgery or radiation therapy might be a better option. For more on these tests, see Risk Groups and Lab Tests to Help Determine Risk for Localized Prostate Cancer.

If your cancer has spread, tests might be done to look for specific gene or protein changes in the cancer cells, which can show if certain <u>targeted therapy drugs</u>⁶ are likely to be helpful in treating the cancer. For example, the cancer cells might be tested for changes (mutations) in the *BRCA* genes or in other genes involved in repairing damaged DNA. If the cells have changes in one of these genes, targeted drugs called PARP inhibitors might be helpful for you.

rectum. The probe gives off sound waves that enter the prostate and create echoes. The probe picks up the echoes, and a computer turns them into a black-and-white image of the prostate.

The test often takes less than 10 minutes and is usually done in a doctor's office or outpatient clinic. You will feel some pressure when the probe is inserted, but it is usually not painful. The area may be numbed before the procedure.

For this test, you are injected with a small amount of low-level radioactive material, which settles in damaged areas of bone throughout the body. A special camera detects the radioactivity and creates a picture of your skeleton.

A bone scan might suggest cancer in the bone, although other non-cancerous conditions such as arthritis can sometimes look similar on the scan. To be sure, other tests, such as plain x-rays, CT or MRI scans, or even a bone biopsy, might be needed.

Positron emission tomography (PET) scan

A <u>PET scan</u>¹⁴ is similar to a bone scan, in that a slightly radioactive substance (known as a **tracer**) is injected into the blood, which can then be detected with a special camera. But PET scans use different tracers that collect mainly in cancer cells.

The most common tracer for standard PET scans is FDG, which is a type of sugar. Unfortunately, this type of PET scan isn't very useful in finding prostate cancer cells in the body. However, newer types of tracers can often be helpful in looking for prostate cancer.

PET scans using newer tracers: Newer tracers that have been found to be better at detecting prostate cancer cells include:

- Fluciclovine F18
- Sodium fluoride F18
- Choline C11

PSMA PET scans: Other newer tracers attach to prostate-specific membrane antigen (PSMA), a protein that is often found in large amounts on prostate cancer cells. These tracers include:

- Ga 68 PSMA-11 (also known as Ga 68 gozetotide, Locametz, and Illuccix)
- 18F-DCFPyl (also known as piflufolastat F 18 or Pylarify)
- 18F-rhPSMA-7.3 (also known as flotufolastat F 18 or Posluma)

These newer types of PET scans are most often used if it's not clear if (or exactly where) prostate cancer has spread. For example, one of these tests might be done if the results of a bone scan aren't clear, or if a man has a rising PSA level after treatment but it's not clear where the cancer is in the body. PSMA PET scans can also be used to help determine if the cancer can be treated with a <u>radiopharmaceutical that targets PSMA¹⁵</u>.

The pictures from a PET scan aren't as detailed as MRI or CT scan images, but they can often show areas of cancer anywhere in the body. Some machines can do a PET scan and either an MRI (PET-MRI) or a CT scan (PET-CT) at the same time, which can give more detail about areas that show up on the PET scan.

Doctors are still learning about the best ways to use these newer types of PET scans, and some of them might not be available yet in all imaging centers.

Computed tomography (CT) scan

A <u>CT scan</u>¹⁶ uses x-rays to make detailed, cross-sectional images of your body. This test isn't often needed for newly diagnosed prostate cancer if the cancer is likely to be confined to the prostate based on other findings (DRE result, PSA level, and Gleason score). Still, it can sometimes help tell if prostate cancer has spread into nearby lymph nodes. If your prostate cancer has come back after treatment, a CT scan can often tell if it is growing into other organs or structures in your pelvis.

CT scans are not as useful as magnetic resonance imaging (MRI) for looking at the prostate gland itself.

Lymph node biopsy

In a lymph node biopsy, also known as **lymph node dissection** or **lymphadenectomy**, one or more <u>lymph nodes</u>¹⁷ are removed to see if they have cancer cells. This isn't done very often for prostate cancer, but it might be used to find out if the cancer has spread from the prostate to nearby lymph nodes.

Lymph node removal during surgery to treat prostate cancer

If surgery is being done to treat prostate cancer and there is more than a very small chance that the cancer might have spread (based on factors such as a high PSA blood level or a high Gleason score from the biopsy), the surgeon may remove lymph nodes in the pelvis during the operation to remove the prostate (**radical prostatectomy.**– See Surgery for Prostate Cancer 18.)

The lymph nodes and the prostate are then sent to the lab to be looked at. The lab results are usually available several days after surgery.

Lymph node biopsy as a separate procedure

- 17. www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html
- 18. www.cancer.org/cancer/types/prostate-cancer/treating/surgery.html
- 19. www.cancer.org/cancer/types/prostate-cancer/treating/radiation-therapy.html

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Prostate Cancer Stages

If you've been diagnosed with prostate cancer, your doctors will try to figure out if it has spread, and if so, how far. This process is called **staging**.

- Determining the stage of prostate cancer
- Stages of prostate cancer

Determining the stage of prostate cancer

The stage of a prostate cancer describes how much cancer is in the body. It's one of the factors used to help determine how best to <u>treat</u>¹ the cancer. Doctors also use a cancer's stage when talking about <u>survival statistics</u>.

The stage is based on tests described in Tests to Diagnose and Stage Prostate Cancer, including the blood PSA level and prostate biopsy results, as well as imaging tests if they are done.

The AJCC TNM staging system

A staging system is a standard way for the cancer care team to describe how far a cancer has spread. The most widely used staging system for prostate cancer is the **AJCC**

category)

- The PSA level at the time of diagnosis
- The **Grade Group** (based on the **Gleason score**), which is a measure of how likely the cancer is to grow and spread quickly. This is determined by the results of the prostate biopsy (or surgery²).

*There are 2 types of T categories for prostate cancer:

- The **clinical T** category (written as **cT**) is your doctor's best estimate of the extent of your cancer, based on the results of the physical exam (including a digital rectal exam) and prostate biopsy, and any imaging tests you have had.
- If you have surgery to remove your prostate, your doctors can also determine the
 pathological T category (written as pT). The pathological T is likely to be more
 accurate than the clinical T, as it is done by examining the entire prostate in the lab.

Numbers or letters after T, N, and M provide more details about each of these factors. Higher numbers mean the cancer is more advanced. Once the T, N, and M categories have been determined, this information is combined (along with the Grade Group and PSA level if they are available) in a process called **stage grouping** to get the overall stage of the cancer.

The main stages of prostate cancer range from I (1) through IV (4). Some stages are split further (IIA, IIB, IIC, etc.). As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV, means cancer has spread more. And within a stage, an earlier letter means a lower stage. Although each person's cancer experience is unique, cancers with similar stages tend to have a similar outlook and are often treated in much the same way.

Stages of prostate cancer

AJCC Stage	Stage grouping	Stage description
	cT1, N0, M0 Grade Group 1 (Gleason score 6	

	OR	1		
	cT2a, N0, M0	The tumor can be felt by digital rectal exam or seen with		
	Grade Group 1 (Gleason score 6 or less) PSA less than 10	imaging, such as transrectal ultrasound, and is in one half or less of only one side (left or right) of the prostate [cT2a]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1, and the PSA level is less than 10.		
I	OR			
	pT2, N0, M0	The prostate has been removed with surgery, and the		
	(Gleason score 6 or less)	tumor was still only in the prostate [pT2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1, and the PSA level is less than 10.		
		The doctor can't feel the tumor or see it with imaging		
	cT1, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA at least 10 but less than 20	such as transrectal ultrasound. (It was either found during a transurethral resection of the prostate (TURP) ⁴ or was diagnosed by needle biopsy done for a high PSA level [cT1].) The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade		
	OR			
	cT2a or pT2, N0, M0	The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound and is in one half or less of only one side (left or right) of the prostate		
	Grade Group 1 (Gleason score 6 or less)	[cT2a]. OR the prostate has been removed with surgery, and the tumor was still only in the prostate [pT2]. The cancer has not spread to nearby lymph		
IIA	PSA at least 10 but less than 20	nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1. The PSA level is at least 10 but less than 20.		
	OR			
	cT2b or cT2c, N0, M0	The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound. It is in more		

	Grade Group 1 (Gleason score 6 or less) PSA less than 20	than half of one side of the prostate [cT2b] or it is in both sides of the prostate [cT2c]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1. The PSA level is less than 20.
IIB	T1 or T2, N0, M0 Grade Group 2 (Gleason score 3+4=7) PSA less than 20	The cancer has not yet spread outside the prostate. It might (or might not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 2. The PSA level is less than 20.
IIC	T1 or T2, N0, M0 Grade Group 3 or 4 (Gleason score 4+3=7 or 8) PSA less than 20	The cancer has not yet spread outside the prostate. It might (or might not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 3 or 4. The PSA level is less than 20.
IIIA	T1 or T2, N0, M0 Grade Group 1 to 4 (Gleason score 8 or less) PSA at least 20	The cancer has not yet spread outside the prostate. It might (or might not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1 to 4. The PSA level is at least 20.
IIIB	T3 or T4, N0, M0 Grade Group 1 to 4 (Gleason score 8 or less) Any PSA	The cancer has grown outside the prostate and might have spread to the seminal vesicles [T3], or it has spread into other tissues next to the prostate, such as the urethral sphincter (muscle that helps control urination), rectum, bladder, and/or the wall of the pelvis [T4]. It has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1 to 4, and the PSA can be any value.
IIIC	Any T, N0, M0 Grade Group 5 (Gleason score 9 or 10)	The cancer might or might not be growing outside the prostate and into nearby tissues [any T]. It has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 5. The PSA can be any value.

	Any PSA	
		The tumor might or might not be growing into tissues near the prostate [any T]. The cancer has spread to
IVA	-	nearby lymph nodes [N1] but has not spread elsewhere
		in the body [M0]. The Grade Group can be any value, and the PSA can be any value.
IVB	Any T, any N, M1	The cancer might or might not be growing into tissues near the prostate [any T] and might or might not have
		spread to nearby lymph nodes [any N]. It has spread to other parts of the body, such as distant lymph nodes,
		bones, or other organs [M1]. The Grade Group can be any value, and the PSA can be any value.

Klein EA. Prostate cancer: Risk stratification and choice of initial treatment. UpToDate.

Risk Groups and Lab Tests to Help Determine Risk from Localized Prostate Cancer

For prostate cancer that has not spread (stage I to III cancers), many doctors now use information about the cancer (such as the T category, initial PSA level, Grade Group, and prostate biopsy results) to place it into a **risk group**. This risk group can then be used to help determine treatment options.

Several expert groups have created risk classification systems for localized prostate cancer. One of the most commonly used systems, developed by the National Comprehensive Cancer Network (NCCN), divides localized prostate cancer into 6 risk groups:

Very-low-risk group

These prostate cancers are small, not felt on exam, can only be found in a small area of the prostate, and have not grown outside the prostate (cT1c). They have a Grade Group of 1 (Gleason score of 6 or less), a low PSA level (less than 10), and few other classification criteria. These cancers usually grow very slowly and almost never cause any symptoms or other health problems.

Low-risk group

Prostate cancers in this group have not yet grown outside of the prostate, have a Grade Group of 1 (Gleason score of 6 or less) and a low PSA level (less than 10), but they are slightly larger (cT1 to cT2a) than very-low-risk cancers. They are unlikely to cause symptoms or other health problems.

Intermediate-risk groups (favorable or unfavorable)

These prostate cancers can be felt on exam or can be seen on an imaging test. The cancer might be found in more than half of one side of the prostate (cT2b) or in both sides of the prostate (cT2c), and/or have a Grade Group of 2 or 3 (Gleason score of 7) and/or a PSA level between 10 and 20 ng/ml.

Additional factors are used to split these prostate cancers into **favorable intermediaterisk** and **unfavorable intermediate-risk** categories.

High-risk group

Prostate cancers in this group have only 1 of these high-risk features (and no very high-risk features [see below]):

The tumor has grown outside the prostate (cT3a).

- The cancer has a Grade Group of 4 or 5 (Gleason score 8 to 10).
- The initial PSA level is more than 20.

Very high-risk group

These prostate cancers have a very high risk for the tumor growing or spreading to nearby lymph nodes (or other parts of the body). These cancers have at least 1 of the following traits:

- The tumor has spread to the seminal vesicles (cT3b) or into other structures next to the prostate (cT4).
- The most common areas of cancer in the biopsy have a Gleason 5 pattern.
- More than 4 biopsy cores are Grade Group 4 or 5 (Gleason score 8 to 10).
- The cancer has 2 or 3 of the features found in the high-risk group (see above).

The risk group can help decide if any further tests should be done, as well as help guide treatment options. Cancers in lower-risk groups have a smaller chance of growing and spreading compared to those in higher-risk groups.

If you have prostate cancer that has not spread to nearby lymph nodes or to other parts of the body, talk to your doctor about which risk group your cancer falls into. This can help you better understand your treatment choices. To learn more about how risk groups are used, see Initial Treatment of Prostate Cancer, by Stage and Risk Group¹.

Lab tests to help determine if localized prostate cancer needs to be treated

Along with the risk groups above, some doctors are now using newer types of lab tests, known as **genomic**, **molecular**, **or proteomic tests**, to help predict how quickly a prostate cancer might grow or spread, and as a result, help decide what treatment options might be best. These tests look at which genes or proteins are active inside the prostate cancer cells.

Examples of such tests include:

• **Decipher:** This test measures the activity of certain genes in prostate cancer cells taken from a biopsy. These are used to create a risk score on a scale from 0 to 1, with a higher score indicating a cancer is more likely to spread to other parts of the

body. This might be helpful in determining the best treatment options. For men who choose surgery (prostatectomy²) to treat their cancer, another version of this test can be used to measure the activity of certain genes in prostate cancer cells from the surgery tissue. This can help determine the risk that the cancer will come back in other parts of the body after surgery, and as a result, if these men should consider further treatment.

- Oncotype DX Prostate: This test measures the activity of certain genes in prostate cancer cells taken from a biopsy and reports it as a score on a scale from 0 to 100. (Higher scores indicate a cancer that is more likely to grow and spread quickly, as well as a higher risk of dying from prostate cancer.)
- Prolaris: This test measures the activity of a different set of genes in prostate cancer cells taken from a biopsy and reports it as a score on a scale from 0 to 10. (Higher scores indicate a cancer that is more likely to grow and spread quickly, as well as a higher risk of dying from prostate cancer.)
- **ProMark:** This test measures the activity of a set of proteins in prostate cancer cells taken from a biopsy and reports it as a score that helps predict how likely a cancer is to grow and spread quickly.

If your doctor suggests using one of these tests to help determine your treatment options, have them explain what it can tell you, as well as how accurate it's likely to be.

These and other new tests are also being studied to look for more areas where they can help with treatment decisions.

Hyperlinks

- 1. www.cancer.org/cancer/types/prostate-cancer/treating/by-stage.html
- 2. www.cancer.org/cancer/types/prostate-cancer/treating/surgery.html

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Klein EA. Prostate cancer: Risk stratification and choice of initial treatment. UpToDate. 2023. Accessed at https://www.uptodate.com/contents/localized-prostate-cancer-risk-stratification-and-choice-of-initial-treatment on July 26, 2023.

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years after being diagnosed.

Where do these numbers come from?

The American Cancer Society relies on information from the SEER (Surveillance, Epidemiology, and End Results) database, maintained by the National Cancer Institute (NCI), to provide survival statistics for different types of cancer.

The SEER database tracks 5-year relative survival rates for prostate cancer in the United States, based on how far the cancer has spread. The SEER database, however, doesn't group cancers by AJCC TNM stages (stage 1, stage 2, stage 3, etc.). Instead it groups cancers into localized, regional, and distant stages.

- Localized: There is no sign that the cancer has spread outside the prostate.
- **Regional:** The cancer has spread outside the prostate to nearby structures or lymph nodes.
- **Distant:** The cancer has spread to other parts of the body, such as the lungs, liver, or bones.

Prostate cancer 5-year relative survival rates

These numbers are based on men diagnosed with prostate cancer between 2013 and 2019.

SEER* Stage	5-year Relative Survival Rate		
Localized	>99%		
Regional	>99%		
Distant	34%		
All SEER stages combined	97%		

Understanding the numbers

 These numbers apply only to the stage of the cancer when it is first diagnosed. They do not apply later on if the cancer grows, spreads, or comes back after treatment.

- These numbers don't take everything into account. Survival rates are grouped based on how far the cancer has spread, but your age and overall health; test results, such as the PSA level and Grade Group of the cancer; how well the cancer responds to treatment; and other factors can also affect your outlook.
- Men now being diagnosed with prostate cancer may have a better outlook than these numbers show. Treatments for prostate cancer have improved over time, and these numbers are based on men who were diagnosed and treated at least 5 years earlier.

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Questions to Ask About Prostate Cancer

If you've been diagnosed with prostate cancer, it's important to have honest, open discussions with your cancer care team.

- When you're told you have prostate cancer
- When deciding on a treatment plan
- During treatment
- After treatment

You should feel free to ask any question, no matter how small it might seem. Here are some questions you might want to ask:

When you're told you have prostate cancer

• What are the chances that the cancer has spread beyond my prostate? If so, is it

still curable?

- Do I need any other tests¹ before we decide on treatment?
- Should I see any other types of doctors before deciding on treatment?
- What is the clinical stage and grade (Gleason score or Grade Group) of my cancer?
 What do those mean for me?
- Which risk group does my cancer fall into? What does this mean?
- If I'm concerned about the <u>costs and insurance coverage</u>² for my diagnosis and treatment, who can help me?

When deciding on a treatment plan

- How likely is my cancer to cause problems if I'm not treated right away?
- Should I consider <u>observation</u> (<u>watchful waiting</u>) or <u>active surveillance</u>³ as an option? Why or why not?
- If I'm choosing to be treated, are both <u>surgery</u>⁴ and <u>radiation therapy</u>⁵ options for me? What are the pros and cons of each?
- What types of radiation therapy might work best for me?
- What other <u>treatment(s)</u>⁶ might be right for me? Why?
- Am I eligible for any <u>clinical trials</u>⁷?
- What risks or side effects should I expect from my treatment options?
- What are the chances that I will have problems with incontinence or impotence?
- What are the chances that I will have other urinary or rectal problems?
- If these side effects happen, are they treatable?
- How quickly do I need to decide on treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How might treatment affect my daily activities?
- What are the chances my cancer will come back with the treatment plans we have discussed? What would be our next step if this happened?

During treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply to you, but getting answers to the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage side effects⁸?
- What symptoms or side effects should I tell you about right away?
- How can I reach you or someone on your team on nights, holidays, or weekends?
- Do I need to change what I eat during treatment⁹?
- Are there any limits on what I can do?
- Do you know of any local or online support groups where I can talk to others who have been through this?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?

After treatment

- Are there any limits on what I can do?
- What symptoms or side effects should I watch for?
- Should I exercise or follow a special diet¹⁰?
- How often will I need follow-up¹¹ exams and tests? What tests will I need?
- How will we know if the cancer has come back 12? What should I watch for?
- What will my options be if the cancer comes back?

Along with these examples, be sure to write down some questions of your own. For instance, you might want to ask about recovery time so that you can plan your work or activity schedule. If you still might <u>want to have children</u>¹³, ask how treatment might affect this.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, can answer some of your questions. To find out more about speaking with your health care team, see
The Doctor-Patient Relationship14.

Hyperlinks

- 1. www.cancer.org/cancer/diagnosis-staging/tests.html
- 2. www.cancer.org/cancer/financial-insurance-matters.html
- 3. www.cancer.org/cancer/types/prostate-cancer/treating/watchful-waiting.html
- 4. www.cancer.org/cancer/types/prostate-cancer/treating/surgery.html

- 5. www.cancer.org/cancer/types/prostate-cancer/treating/radiation-therapy.html
- 6. <u>www.cancer.org/cancer/types/prostate-cancer/treating.html</u>
- 7. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 8. www.cancer.org/cancer/managing-cancer/side-effects.html
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- 12. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 13. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects.html</u>
- 14. <u>www.cancer.org/cancer/managing-cancer/finding-care/the-doctor-patient-relationship.html</u>

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